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**Polysialic acid, a glycan with highly restricted expression, is found on human and murine leukocytes and modulates immune responses.**

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**Public Summary:**

**Scientific Abstract:**

Polysialic acid (polySia) is a large glycan with restricted expression, typically found attached to the protein scaffold neural cell adhesion molecule (NCAM). PolySia is best known for its proposed role in modulating neuronal development. Its presence and potential functions outside the nervous systems are essentially unexplored. Herein we show the expression of polySia on hematopoietic progenitor cells, and demonstrate a role for this glycan in immune response using both acute inflammatory and tumor models. Specifically, we found that human NK cells modulate expression of NCAM and the degree of polymerization of its polySia glycans according to activation state. This contrasts with the mouse, where polySia and NCAM expression are restricted to multipotent hematopoietic progenitors and cells developing along a myeloid lineage. Sialyltransferase 8Sia IV(-/-) mice, which lacked polySia expression in the immune compartment, demonstrated an increased contact hypersensitivity response and decreased control of tumor growth as compared with wild-type animals. This is the first demonstration of polySia expression and regulation on myeloid cells, and the results in animal models suggest a role for polySia in immune regulation.

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